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PRINCIPLES OF NEURAL SCIENCE

SECOND EDITION

Edited by

ERIC R. KANDEL, M.D.

and

JAMES H. SCHWARTZ, M.D., PH.D.

Center for Neurobiology and Behavior
College of Physicians & Surgeons of Columbia University
and
Howard Hughes Medical Institute

Art rendered by Jonathan Dimes

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Director of Editing Barbara A. Conover
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Art rendered by Jonathan Dimes
Department of Art as Applied to Medicine
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differences among multipolar cells are due largely to variations in two features: the number and length of the dendrites, and the length of the axon. The number and extent of dendritic processes in a given cell correlate with the number of synaptic contacts that other neurons make on that cell. A spinal motor cell, whose dendrites are moderate in both number and extent, receives roughly 10,000 contacts. The large dendritic tree of the Purkinje cell of the cerebellum receives approximately 150,000 contacts!

The length of the axon reflects the signaling function of a neuron. Neurons with long axons (sometimes called Golgi type I cells) carry information from one brain region to another; they serve as *projection* or *relay neurons*. Neurons with short axons (Golgi type II cells) primarily process information within a small, limited region of the brain. These nerve cells serve as *local interneurons* in various nuclei of the brain and in reflex pathways.

Glial Cells

There are between 10 and 50 times more glial cells than neurons in the central nervous system. In addition to being ubiquitous, glial cells are typically small and do not generate active electrical signals as neurons do. Glial cells are found between nerve cell bodies and also between axons. As a group, the various types of glial cells are thought to serve six distinct functions:

1. Glia (Greek, meaning glue) are supporting elements that provide firmness and structure for the brain, a role played by connective tissue cells in other parts of the body. They also segregate and occasionally insulate groups of neurons from each other.
2. Some glial cells are scavengers that remove debris after neuronal death or injury.
3. Certain glial cells provide myelin, the insulating sheath that covers some axons.
4. Glial cells buffer the K^+ concentration of the extracellular space and help to remove chemical transmitters released by neurons.
5. During development, certain classes of glial cells guide the migration of neurons and, possibly, direct the outgrowth of axons.
6. There is suggestive evidence that some glial cells have nutritive functions for nerve cells, although this has been difficult to demonstrate conclusively.

As we shall see below, different aspects of these functions are carried out by different types of glial cells.

Glial cells are generally divided into two major classes: *macroglia* (astrocytes, oligodendrocytes, and ependymal cells), and *microglia* (an assortment of phagocytic cells that are mobilized after injury, infection, or disease).

The origin of microglia is still not known. Until recently they were thought to derive from blood-borne macrophages but now are believed to derive from ectoderm, like the nervous system itself, and to proliferate as needed from a resting population of immature glial precursor cells. Because microglia are phagocytes and belong to a physiologically distinct class of cells, unrelated to the nervous system, we shall not consider them further.

The two predominant types of macroglia are *astrocytes*, characterized by many processes, and *oligodendrocytes*, with few processes (Figure 2–3A and B). The *ependymal cells*, a third type, line the central canal system of the brain and spinal cord.

Astrocytes are star-shaped cells with small, irregularly shaped cell bodies and numerous extensions that ramify between the processes of nerve cells. They are commonly divided into two subclasses: fibrous and protoplasmic (Figure 2–3B). *Fibrous astrocytes* contain many filaments and are found in areas of the central nervous system containing mostly axons. These regions are called *white matter* because of the color of myelinated axons in unstained, freshly cut brain sections. The *protoplasmic astrocytes* have shorter and stouter processes that contain few filaments; these astrocytes are associated with nerve cell bodies, dendrites, and particularly synapses, which they characteristically envelop. The regions in which protoplasmic astrocytes predominate are called *gray matter* because large collections of nerve cell bodies and dendrites appear grayish in brain sections.

Astrocytes probably serve a number of functions. The processes of fibrous and protoplasmic astrocytes have end-feet that contact blood capillaries on the one hand and neurons on the other, suggesting that astrocytes have a nutritive function (Figure 2–3C). After injury, astrocytes and microglia remove neuronal debris and help seal off damaged brain tissue. Furthermore, as first shown by Stephen Kuffler, John Nicholls, and their colleagues, the resting potential of astrocytes is sensitive to small changes in K^+ concentration in the extracellular space. By taking up the excess extracellular K^+, astrocytes are thought to buffer the extracellular K^+ concentration so as to protect the membrane potential of neurons from the depolarization that might result if K^+ accumulated after repeated neuronal firing. Similarly, the protoplasmic astrocytes that surround the synaptic region have a high-affinity uptake mechanism for certain neurotransmitter substances such as γ-aminobutyric acid (GABA) and serotonin, and are thus able to remove them from the synaptic cleft.

Oligodendrocytes are small glial cells with few processes (Figure 2–3A). The one known function of oligodendrocytes is to contribute the myelin sheath to the axon, which greatly enhances the axon's conduction efficiency. They form this sheath by wrapping their membranous processes around the axon in a tight spiral. Oligodendrocytes are found in the central nervous system; their counterpart in the peripheral nervous system is the *Schwann cell*, which forms the myelin sheath around the axons of peripheral nerves. These two sheathing cells differ in that the oligodendrocyte envelops several axons in the central nervous system, whereas the Schwann cell is associated with only one axon in the periphery. Myelination will be considered in greater detail in Chapter 3.